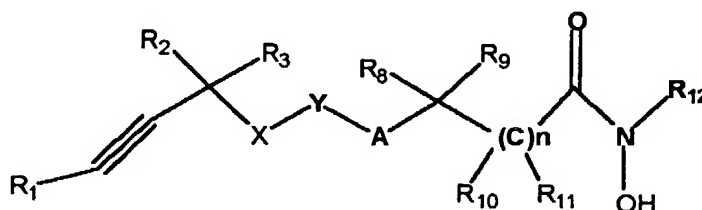


APPENDIX
AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

AMENDMENT TO THE CLAIMS

Claim 1 (Currently amended). A compound of formula



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wherein:

- R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;
- R_2 and R_3 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;
- R_7 is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)- R_1 , -SO₂- R_1 , -C(O)-NHR₁, -C(O)NR₃R₆, -C(O)R₁NR₃R₆, -C(O)-OR₁, or -C(NH)-NH₂;
- R_5 and R_6 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, aralkyl, heteroaryl, heteroaralkyl or -C₄-C₈-cycloheteroalkyl;
- R_8 , R_9 , R_{10} , and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R_8 and R_9 , R_9 and R_{10} or R_{10} and R_{11} , R_8 and R_9 , R_9 and R_{10} or R_{10} and R_{11} , together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;
- R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;
- A is O, S, SO, SO₂, NR₇, or CH₂;

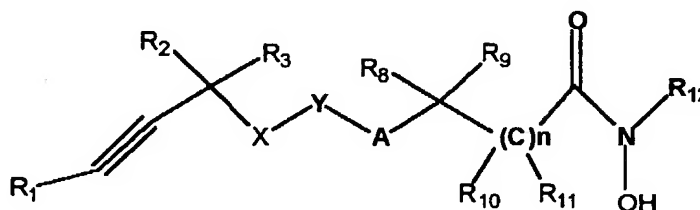
X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and
with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom
to which they are attached may not form a piperdiny or tetrahydropyranyl ring; and
n is 0-2; or a pharmaceutically acceptable salt thereof.

Claim 2 (Previously amended). A compound of Claim 1 wherein Y is phenyl, pyridyl, thienyl,
furanyl, imidazolyl, triazolyl or thiadiazolyl.

Claim 3 (Cancelled).

Claim ³ (Currently amended). A method of treating a pathological condition or disorder which
requires inhibition of TNF- α converting enzyme (TACE) in a mammal in need thereof which
comprises administering to said mammal a therapeutically effective amount of a compound having
the formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl
of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6
carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁,
-SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, or -C(NH)-NH₂;

R₅ and R₆ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-6
carbon atoms, aryl, aralkyl, heteroaryl, heteroaralkyl or -C₄-C₈-cycloheteroalkyl;

R_8 , R_9 , R_{10} , and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R_8 and R_9 , R_9 and R_{10} or R_{10} and R_{11} , R_8 and R_9 , R_9 and R_{10} or R_{10} and R_{11} , together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

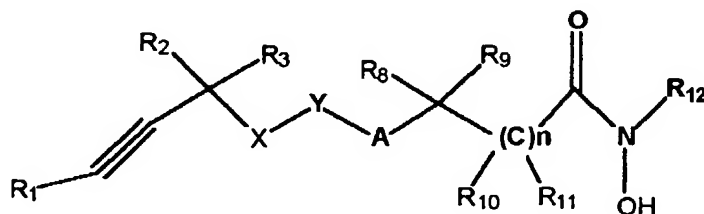
X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

cont'd
Claim ^{if} 5 (Original). The method of Claim ³ 4 wherein the condition treated is rheumatoid arthritis, graft rejection, cachexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease or HIV infection.

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Claim ⁵ 6 (Currently amended). A pharmaceutical composition comprising a therapeutically effective amount of a compound having the formula



I

wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, or -C(NH)-NH₂;

~~R₅ and R₆ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, aralkyl, heteroaryl, heteroaralkyl or -C₄-C₈-cycloheteroalkyl;~~

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs ~~R₈ and R₉~~, ~~R₉ and R₁₀~~ or ~~R₁₀ and R₁₁~~, ~~R₈ and R₉~~, ~~R₉ and R₁₀~~ or ~~R₁₀ and R₁₁~~, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;

R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyll or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.